REMARKS

Claims 6 and 8-10 are pending in the instant application. Claims 6 and 10 have been rejected. Claims 6 and 8-10 are objected to. After entry of these arguments, Claims 6 and 8-10 will remain pending.

Applicants would like to thank Examiner Havlin for discussing the pending application with their representative Nicole Beeler on November 03, 2009. The Examiner's guidance is appreciated.

Rejection of Claims 6 and 10 under 35 USC §103(a)

The Examiner has rejected Claims 6 and 10 under 35 U.S.C. §103(a), as allegedly being unpatentable over Sangwan et al., *Chimica Acta Turcica 11 (1983).*

Applicants respectfully traverse this rejection. Applicants do not believe that the Sangwan reference is analogous art. The present invention claims novel 2,5-difulouro substituted dihydropyrazoles, which are useful in the treatment of cancer by inhibiting kinesin spindle protein. The ability to inhibit the kinsein spindle protein is affected by the particular substitution pattern on the phenyl ring.

Sangwan does not teach difluoro substituted dihydropyrazoles; rather, Sangwan teaches substituted 4,5-dihydropyrazoles that are useful as antimicrobial agents. Presumably, the ability to treat bacterial and fungal infections is affected by the particular substitution pattern on the phenyl rings.

The pharmaceutical sciences are highly unpredictable, and it is difficult to predict the activity of a compound merely by looking at it. After reviewing the Sangwan reference, one skilled in the art would not expect the compounds described therein to be effective for any other use that as an antimicrobial agent. The Sangwan reference does not teach the use of dihydropyrazoles for the treatment of cancer, and as such, one skilled in the art would not be motivated to use the compounds disclosed therein for the treatment of cancer via inhibition of kinesin spindle proteins.

Applicants respectfully traverse this rejection. Drug discovery and design is a complex process, and the activity of seemingly similar compounds can be vastly different when tested. Applicants maintain that the 2,5-halo analogs of the instant invention are not obvious in light of the Sangwan reference because they are more potent inhibitors of KSP than the compound in the Sangwan reference, which has a 2-hydroxy, 5-bromo substitution pattern. As explained in a paper authored by many of the inventors of the instant application, the 2,5-

difluoro derivative displayed surprising potency when compared to other halogenated and nonhalogenated analogs, *see* C.D. Cox, et al., "Kinesin spindle protein (KSP) inhibitors. Part 1: The discovery of 3,5-diaryl-4,5-dihydropyrazoles as potent and selective inhibitors of the mitotic kinesin KSP," *Bioorganic & Medicinal Chemistry Letters* 15 (2005)2041-2045 (copy enclosed). As shown on page 2042, in Table 1, the 2-methoxy analog was much less active (>50,000 nM) than the di-halogenated analogs. In fact, the authors note that modest modifications from halo, such as methyl, methoxy and trifluoromethyl resulted in substantial losses in potency. Thus, the boost in potency from using dihalo analogs could not have been predicted and was in fact an unexpected result.

In light of these arguments, Applicants respectfully request the rejections of Claims 6 and 10 under 35 USC §103(a), be withdrawn.

Objection to Claims 8 and 10

The Examiner has objected to Claims 8 and 10 as being dependent on a rejected base claim. Applicants believe that Claims 6 and 8-10 are in condition for allowance, and respectfully request that the objection to Claims 8 and 10 be withdrawn.

If a telephonic communication with the Applicants' representative will advance the prosecution of the instant application, please telephone the representative indicated below. Applicants believe no additional fees are due but the Commissioner is authorized to charge any fees required in connection with this response to Merck Deposit Account No. 13-2755.

Respectfully submitted,

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Date: November 10, 2009

Enclosures: (1) C.D. Cox, *et al., Bioorg. Med. Chem. Lett.* **15** (2005) 2041-2045